

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1-8. (Cancelled)

9. (Previously Presented) A method for inhibiting synovial cell growth, comprising administering to a patient in need thereof a pharmaceutical composition comprising humanized PM-1 antibody and a physiologically acceptable carrier, wherein said humanized PM-1 antibody comprises

(A) L chains of an antibody to a human IL-6 receptor, each comprising:

(1) a variable (V) region of a light (L) chain of an antibody to the human IL-6 receptor having the following structure:

FR1¹-CDR1¹-FR2¹-CDR2¹-FR3¹-CDR3¹-FR4¹

wherein CDR1¹, CDR2¹ and CDR3¹ represent a set of three complementarity determining regions comprising a set of the following amino acid sequences:

CDR1¹ Arg Ala Ser Gln Asp Ile Ser Ser Tyr Leu Asn (SEQ ID NO: 2)

CDR2¹ Tyr Thr Ser Arg Leu His Ser (SEQ ID NO: 3)

CDR3¹ Gln Gln Gly Asn Thr Leu Pro Tyr Thr (SEQ ID NO: 4); and the FR1¹, FR2¹, FR3¹ and FR4¹ comprise a set of the following amino acid sequences:

FR1¹ Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys (SEQ ID NO: 5)

FR2¹ Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr (SEQ ID NO: 6)

FR3¹ Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala Thr Tyr Tyr Cys (SEQ ID NO: 7)

FR4¹ Phe Gly Gln Gly Thr Lys Val Glu Ile Lys (SEQ ID NO: 8);

or

FR1¹ Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys (SEQ ID NO: 5)

FR2¹ Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr (SEQ ID NO: 6)

FR3¹ Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala Thr Tyr Tyr Cys (SEQ ID NO: 9)

FR4¹ Phe Gly Gln Gly Thr Lys Val Glu Ile Lys (SEQ ID NO: 8);

and

(2) a C region of an L chain of a human antibody C κ ; and

(B) H chains of an antibody to the human IL-6 receptor, each comprising:

(1) a V region of a heavy (H) chain of an antibody to the human IL-6 receptor having the following structure:

FR1²-CDR1²-FR2²-CDR2²-FR3²-CDR3²-FR4²

wherein CDR1², CDR2² and CDR3² represent a set of three complementarity determining regions comprising a set of the following amino acid sequences:

CDR1² Ser Asp His Ala Trp Ser (SEQ ID NO: 10)

CDR2² Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu Lys Ser (SEQ ID NO: 11)

CDR3² Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr (SEQ ID NO: 12);

and the FR1², FR2², FR3² and FR4² comprise a set of the following amino acid sequences:

FR1² Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg
Pro Ser Gln Thr Leu Ser Leu Thr Cys Thr Val Ser Gly
Tyr Ser Ile Thr (SEQ ID NO: 13)
FR2² Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile
Gly (SEQ ID NO: 14)
FR3² Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe
Ser Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala
Val Tyr Tyr Cys Ala Arg (SEQ ID NO: 15) and
FR4² Trp Gly Gln Gly Ser Leu Val Thr Val Ser Ser (SEQ ID
NO: 16);

and

(2) a C region of an H chain of a human antibody C γ .

10. (Cancelled)

11. (Previously Presented) The method according to claim 9, wherein the patient is a human.

12. (Previously Presented) The method according to claim 11, wherein the antibody is administered in four divided doses from about 1 to 1000 mg.

13. (Previously Presented) A method of treating chronic rheumatoid arthritis, comprising administering to a patient in need thereof a pharmaceutical composition comprising humanized PM-1 antibody and a physiologically acceptable carrier, wherein said humanized PM-1 antibody comprises

(A) L chains of an antibody to a human IL-6 receptor, each comprising:

(1) a variable (V) region of a light (L) chain of an antibody to the human IL-6 receptor having the following structure:

FR1¹-CDR1¹-FR2¹-CDR2¹-FR3¹-CDR3¹-FR4¹

wherein CDR1¹, CDR2¹ and CDR3¹ represent a set of three complementarity determining regions comprising a set of the following amino acid sequences:

CDR1¹ Arg Ala Ser Gln Asp Ile Ser Ser Tyr Leu Asn (SEQ ID NO: 2)

CDR2¹ Tyr Thr Ser Arg Leu His Ser (SEQ ID NO: 3)

CDR3¹ Gln Gln Gly Asn Thr Leu Pro Tyr Thr (SEQ ID NO: 4); and the FR1¹, FR2¹, FR3¹ and FR4¹ comprise a set of the following amino acid sequences:

FR1¹ Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys (SEQ ID NO: 5)

FR2¹ Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr (SEQ ID NO: 6)

FR3¹ Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala Thr Tyr Tyr Cys (SEQ ID NO: 7)

FR4¹ Phe Gly Gln Gly Thr Lys Val Glu Ile Lys (SEQ ID NO: 8);

or

FR1¹ Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys (SEQ ID NO: 5)

FR2¹ Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr (SEQ ID NO: 6)

FR3¹ Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Thr Asp Tyr Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala Thr Tyr Tyr Cys (SEQ ID NO: 9)

FR4¹ Phe Gly Gln Gly Thr Lys Val Glu Ile Lys (SEQ ID NO: 8);

and

(2) a C region of an L chain of a human antibody C κ ; and

(B) H chains of an antibody to the human IL-6 receptor, each comprising:

(1) a V region of a heavy (H) chain of an antibody to the human IL-6 receptor having the following structure:

FR1²-CDR1²-FR2²-CDR2²-FR3²-CDR3²-FR4²

wherein CDR1², CDR2² and CDR3² represent a set of three complementarity determining regions comprising a set of the following amino acid sequences:

CDR1² Ser Asp His Ala Trp Ser (SEQ ID NO: 10)

CDR2² Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu Lys Ser (SEQ ID NO: 11)

CDR3² Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr (SEQ ID NO: 12);

and the FR1², FR2², FR3² and FR4² comprise a set of the following amino acid sequences:

FR1² Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr (SEQ ID NO: 13)

FR2² Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile Gly (SEQ ID NO: 14)

FR3² Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg (SEQ ID NO: 15) and

FR4² Trp Gly Gln Gly Ser Leu Val Thr Val Ser Ser (SEQ ID NO: 16);

and

(2) a C region of an H chain of a human antibody C γ .

14. (Previously Presented) The method according to claim 13, wherein the antibody suppresses abnormal growth of synovial cells.

15. (Cancelled)

16. (Previously Presented) The method according to claim 13, wherein the patient is a human.

17. (Previously Presented) The method according to claim 16, wherein the antibody is administered in four divided doses from about 1 to 1000 mg.

18. (Cancelled)

19. (New) A method for inhibiting synovial cell growth, comprising administering to a patient in need thereof a pharmaceutical composition comprising humanized antibody and a physiologically acceptable carrier, wherein said humanized antibody comprises

(A) L chains of an antibody to a human IL-6 receptor, each comprising:

(1) a variable (V) region of a light (L) chain of an antibody to the human IL-6 receptor having the following structure:

FR1¹-CDR1¹-FR2¹-CDR2¹-FR3¹-CDR3¹-FR4¹

wherein CDR1¹, CDR2¹ and CDR3¹ represent a set of three complementarity determining regions comprising a set of the following amino acid sequences:

CDR1¹ Arg Ala Ser Gln Asp Ile Ser Ser Tyr Leu Asn (SEQ ID NO: 2)

CDR2¹ Tyr Thr Ser Arg Leu His Ser (SEQ ID NO: 3)

CDR3¹ Gln Gln Gly Asn Thr Leu Pro Tyr Thr (SEQ ID NO: 4); and the FR1¹, FR2¹, FR3¹ and FR4¹ comprise a set of the following amino acid sequences:

FR1¹ Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys (SEQ ID NO: 5)

FR2¹ Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr (SEQ ID NO: 6)

FR3¹ Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala Thr Tyr Tyr Cys (SEQ ID NO: 7)

FR4¹ Phe Gly Gln Gly Thr Lys Val Glu Ile Lys (SEQ ID NO: 8);

or

FR1¹ Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys (SEQ ID NO: 5)

FR2¹ Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr (SEQ ID NO: 6)

FR3¹ Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala Thr Tyr Tyr Cys (SEQ ID NO: 9)

FR4¹ Phe Gly Gln Gly Thr Lys Val Glu Ile Lys (SEQ ID NO: 8);

and

(2) a C region of an L chain of a human antibody C κ ; and

(B) H chains of an antibody to the human IL-6 receptor, each comprising:

(1) a V region of a heavy (H) chain of an antibody to the human IL-6 receptor having the following structure:

FR1²-CDR1²-FR2²-CDR2²-FR3²-CDR3²-FR4²

wherein CDR1², CDR2² and CDR3² represent a set of three complementarity determining regions comprising a set of the following amino acid sequences:

CDR1² Ser Asp His Ala Trp Ser (SEQ ID NO: 10)

CDR2² Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu Lys Ser (SEQ ID NO: 11)

CDR3² Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr (SEQ ID NO: 12);

and the FR1², FR2², FR3² and FR4² comprise a set of the following amino acid sequences:

FR1² Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg
Pro Ser Gln Thr Leu Ser Leu Thr Cys Thr Val Ser Gly
Tyr Ser Ile Thr (SEQ ID NO: 13)
FR2² Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile
Gly (SEQ ID NO: 14)
FR3² Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe
Ser Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala
Val Tyr Tyr Cys Ala Arg (SEQ ID NO: 15) and
FR4² Trp Gly Gln Gly Ser Leu Val Thr Val Ser Ser (SEQ ID
NO: 16);

and

(2) a C region of an H chain of a human antibody C γ .

20. (New) The method according to claim 19, wherein the patient is a human.

21. (New) The method according to claim 20, wherein the antibody is administered in four divided doses from about 1 to 1000 mg.

22. (New) A method of treating chronic rheumatoid arthritis, comprising administering to a patient in need thereof a pharmaceutical composition comprising humanized antibody and a physiologically acceptable carrier, wherein said humanized antibody comprises

(A) L chains of an antibody to a human IL-6 receptor, each comprising:

(1) a variable (V) region of a light (L) chain of an antibody to the human IL-6 receptor having the following structure:

FR1¹-CDR1¹-FR2¹-CDR2¹-FR3¹-CDR3¹-FR4¹

wherein CDR1¹, CDR2¹ and CDR3¹ represent a set of three complementarity determining regions comprising a set of the following amino acid sequences:

CDR1¹ Arg Ala Ser Gln Asp Ile Ser Ser Tyr Leu Asn (SEQ ID NO: 2)

CDR2¹ Tyr Thr Ser Arg Leu His Ser (SEQ ID NO: 3)

CDR3¹ Gln Gln Gly Asn Thr Leu Pro Tyr Thr (SEQ ID NO: 4);

and the FR1¹, FR2¹, FR3¹ and FR4¹ comprise a set of the following amino acid sequences:

FR1¹ Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys (SEQ ID NO: 5)
FR2¹ Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr (SEQ ID NO: 6)
FR3¹ Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala Thr Tyr Tyr Cys (SEQ ID NO: 7)
FR4¹ Phe Gly Gln Gly Thr Lys Val Glu Ile Lys (SEQ ID NO: 8);

or

FR1¹ Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys (SEQ ID NO: 5)
FR2¹ Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr (SEQ ID NO: 6)
FR3¹ Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala Thr Tyr Tyr Cys (SEQ ID NO: 9)
FR4¹ Phe Gly Gln Gly Thr Lys Val Glu Ile Lys (SEQ ID NO: 8);

and

(2) a C region of an L chain of a human antibody C κ ; and

(B) H chains of an antibody to the human IL-6 receptor, each comprising:

(1) a V region of a heavy (H) chain of an antibody to the human IL-6 receptor having the following structure:

FR1²-CDR1²-FR2²-CDR2²-FR3²-CDR3²-FR4²

wherein CDR1², CDR2² and CDR3² represent a set of three complementarity determining regions comprising a set of the following amino acid sequences:

CDR1² Ser Asp His Ala Trp Ser (SEQ ID NO: 10)
CDR2² Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu Lys Ser (SEQ ID NO: 11)
CDR3² Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr (SEQ ID NO: 12);

and the FR1², FR2², FR3² and FR4² comprise a set of the following amino acid sequences:

FR1² Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr (SEQ ID NO: 13)
FR2² Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile Gly (SEQ ID NO: 14)
FR3² Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg (SEQ ID NO: 15) and
FR4² Trp Gly Gln Gly Ser Leu Val Thr Val Ser Ser (SEQ ID NO: 16);

and

(2) a C region of an H chain of a human antibody C γ .

23. (New) The method according to claim 22, wherein the antibody suppresses abnormal growth of synovial cells.

24. (New) The method according to claim 22, wherein the patient is a human.

25. (New) The method according to claim 24, wherein the antibody is administered in four divided doses from about 1 to 1000 mg.